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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,669	01/14/2004	Kurt Lang	CIBT-P02-092	7295
28120	7590	10/18/2005	EXAMINER	
FISH & NEAVE IP GROUP ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			HOWARD, ZACHARY C	
			ART UNIT	PAPER NUMBER
			1646	

DATE MAILED: 10/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/757,669

Applicant(s)

LANG ET AL.

Examiner

Zachary C. Howard

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) 1,5 and 6 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-4,7 and 8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-8 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 January 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 1/14/2004.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 2-4, 7 and 8, in the reply filed on 7/28/2005 is acknowledged.

The traversal is on the ground(s) that the inventions of Groups I and II are directed to overlapping subject matter related to hedgehog proteins and therefore can be examined simultaneously without significant additional burden.

This is not found persuasive because under current examination guidelines, the examiner may require restriction between product and process claims (see the restriction requirement mailed 6/28/2005, pages 2-3). Where Applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04.

In the instant application, Applicants have elected the product claims (Group I). As discussed in the restriction requirement of 6/6/05, Group I is a distinct invention from Group II because the product of Group I can be made by a materially different method from that of Group II. Serious burden was shown in the original requirement by the separate classification of Group I from Group II. The restriction is proper because a search for the product of Group I and the method of Group II would not be coextensive.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 5 and 6 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/28/2005.

Claims 2-4, 7 and 8 are under consideration.

Claim Objections

Claims 2, 7 and 8 are objected to because the claims use the acronym "hh". Use of acronyms results in indefinite language because the acronyms used to define proteins can be subject to change or reference more than one protein. Therefore, when used for the first time scientific terms should be completely spelled out.

Claims 7 and 8 are objected to because the claims depend from non-elected inventions. Each of claim 7 and 8 depend from claim 1, which is drawn to a non-elected invention.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, 1st paragraph, scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 and 8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for the production of a composition comprising a hedgehog mutant and a pharmaceutical auxiliary substance or suramin or a biocompatible matrix or a sequestering agent, does not reasonably provide enablement for a process for the production of a pharmaceutical composition comprising a hedgehog mutant and said substances. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 7 and 8 are directed to a process for the production of a pharmaceutical composition that combines either a hh mutant of claim 1 with a pharmaceutical substance or suramin (claim 7); or a hh mutant with a biocompatible matrix and/or a sequestering agent (claim 8).

The specification teaches said compositions comprising a hh mutant of claim 1 on page 7 of the specification. However, the specification does not teach how to use the "pharmaceutical" composition without undue experimentation for the treatment of a disease in an animal. The specification teaches (pg 7) that the pharmaceutical composition can be administered systemically or locally. The specification further teaches that the protein of the invention "can be used advantageously to induce chondrocytes and osteocytes in an osteoinductive pharmaceutical composition." The specification provides several references that teach osteoinductive pharmaceutical compositions. However, these references are not directed to compositions comprising the hedgehog protein. There are no working examples directed to a particular disorder in an animal or administration of the pharmaceutical composition comprising a hh protein. (Note, this issue could be overcome by deleting the word "pharmaceutical" from the claims.)

Due to the large quantity of experimentation necessary to determine the quantity of hh mutant pharmaceutical composition to be administered, the most effective administration route, and the duration of the treatment, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of the effects of the hh mutant *in vivo*, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is indefinite because it is not clear what is meant by a "in a fermentation". Specifically, the claim recites "...by expressing a gene which codes for a hedgehog protein in a Baculovirus expression system in a fermentation for a period of 24 to 27 hours..." This claim would be rendered definite, for example, by amending the claim to recite "...in a fermentation system..."

Claim 2 is also indefinite because it is not clear what activity is being referred to in the following phrases: "stabilized with respect to its activity"; "is inactivated when 8 or more amino acids are cleaved N-terminally"; or "is inactivated by 90% or more when incubated with...". Furthermore, with regard to "induces an activity for alkaline phosphatase of..." it is unclear how this activity is determined.

Claim 3 is indefinite because the metes and bounds of the phrase "lower ionic strength" cannot be determined. It is not clear what conditions are encompassed by this phrase.

Claim 8 is indefinite because the elements recited in the claims do not constitute proper Markush groups. The claims are indefinite in the alternative use of "and/or" because it is not clear what controls which of these limitations. See MPEP § 2173.05(h).

Claims 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims do not contain any method steps for the process.

Double Patenting

Claims 2-4, 7 and 8 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 and 13 of copending Application No. 09198975.

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Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 2-4 of the instant application and claims 11 and 13 of '975 are each drawn to a process for production of a post-translationally processed hedgehog protein mutant. The protein produced in each case has identical characteristics, except that the protein produced by the method of claims 11 and 13 of the '975 application has "at least 50-fold activity compared to the corresponding recombinant hedgehog protein isolated from the cytoplasm of E. coli, wherein said activity is measured as alkaline phosphatase induction in a C3H10T1/2 cell test". However, the specification of each application is identical, and the only disclosed protein that has the other disclosed characteristics (molecular weight, etc.) also has 50-fold greater activity (see page 16). Furthermore, instant claim 2 includes the limitation that the gene is expressed in a baculovirus expression system for a period of 24 to 27 hours, whereas claim 11 of '975 is silent as to the length of the expression. However, the specification reveals that 24-27 hours is the optimal length of time for expression of the hedgehog protein. Therefore, the methods of claims 2 and 11 are not patentably distinct from each other because they are each drawn to a process that is inherently the same as the other process.

Instant claims 3 and 4 include the limitations that the process further includes dialysis against lower ionic strengths after chromatography on heparin-Sepharose (claim 3) and wherein the dialysis of claim 3 is carried out in 10-100 mmol/liter sodium chloride (claim 4). Claim 13 of '975 includes the limitation that the process of claim 11 further comprises dialyzing the protein against a buffer having 10-100 mmol/l sodium chloride. Therefore, the further limitation of instant claim 4 and claim 13 of '975 are identical, and the further limitation of claim 3 includes a genus of buffers of which the buffer of claim 13 of '975 is a species that falls within the genus. Therefore, the methods of instant claims 3 and 4 are not patentably distinct from the method of claim 13 of '975.

Instant claims 7 and 8 are each directed to a process for the production of a pharmaceutical composition that combines either a hh mutant of claim 1 with a pharmaceutical substance or suramin (claim 7); or a hh mutant with a biocompatible matrix and/or a sequestering agent (claim 8). Claim 13 of '975 results in a hedgehog protein in buffer; therefore the process of instant claim 7 is a genus claim and claim 13 of '975 is a species within this genus; therefore the claims are not patentably distinct. The method of claim 11 of '975 includes binding the protein to herapin-sepharose, which meets the limitation of a sequestering agent; therefore the process of instant claim 8 is a genus claims and claim 11 of '975 is a species within this genus; therefore the claims are not patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Art of Note

The following patents were found during the art search, and while not relied upon for a rejection, are considered pertinent to the instant application:

a. Ingham et al., U. S. Patent No. 5,844,079, published 12/1/1998 and filed 12/14/1994. Ingham teaches expressing hedgehog protein in a baculoviral system. However, one of skill in the art, following the teachings of Ingham by expressing hedgehog using the baculovirus system, would not necessarily realize that two forms of hedgehog were produced, and further if one of skill in the art were to realize that two forms were present, then one of skill in the art would not necessarily be motivated to distinguish the activities of the two species of hedgehog.

b. Pepinsky et al., U. S. Patent 6,444,793, published 9/3/2002 and filed 6/3/1999 (cited by Applicants on the 1/14/2004 IDS as reference AB). In Example I beginning on col 42, Pepinsky teaches a process for the production of a post

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translationally processed hedgehog protein in a baculovirus expression fermentation system, purifying the cell supernatant in the presence of a proteinase inhibitor (e.g. PMSF) and a non-ionic detergent (e.g. Triton X-100). Further the expressed protein corresponded to a molecular weight of 20 kD in SDS-PAGE. However, Pepinsky teach that the protein is modified with a cholesterol moiety and a palmitic acid moiety (e.g. col 44), and therefore does not anticipate the present claims, which require that the hedgehog protein produced is not modified by cholesterol.

Conclusion

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 571-272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Bridget E. Bunner

**BRIDGET BUNNER
PATENT EXAMINER**